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(54) **Title of the Invention** **Plastic Injection Device**

(57) **Abstract**

Constitution Plastic injection device with its syringe made of a random copolymer of ethylene and a tetracyclo[4.4.0.$1^{2.5}$.$1^{7.10}$-3-dodecene derivative.

Effects This plastic injection device shows an excellent water vapor blocking property, chemical reagent resistance, transparency and dimensional stability and shows no seepage of an eluate from the syringe to a liquid medicine. Furthermore, the inner surface of the syringe and the outer surface of the gasket of the plastic injection device of the present invention are made of a roughened surface and thus it can allow the flow of a liquid medicine into and out of the syringe part with a low sliding resistance without coating the gasket with a silicone liquid.

Scope of the Patent Claims

1. Plastic injection device with its syringe made of a random copolymer of ethylene and a tetracyclo[$4.4.0.1^{2.5}.1^{7.10}$]-3-dodecene derivative.

2. Plastic injection device in accordance with claim 1, in which the inner surface of the syringe is made of a roughened surface.

3. Plastic injection device in accordance with claim 1 or 2, in which the average roughness of the roughened surface is greater than 0.1 μm.

4. Plastic injection device in accordance with any of the claims 1-3, in which the gasket is made of polyethylene.

5. Plastic injection device in accordance with any of the claims 1-4, in which the outer surface of the gasket is made of a roughened surface.

Detailed Description of the Invention

[0001]

Field of Industrial Application The present invention pertains to a plastic injection device with excellent transparency with decreased seepage of an eluate from the inner part of the syringe.

[0002]

Prior Art An injection device made of plastics has been used widely because it can prevent a risk of breakage that may occur during the use of an injection device made of glass. However, some liquid medicines contained in the injection device may undergo a chemical reaction with the plastics and the eluate from the plastics may seep into the liquid medicine. This is especially so in the case of a pre-filled syringe in which a liquid medicine is pre-stored in a cartridge, i.e., a long-term storage of a liquid medicine in a plastic injection device may result in seepage of the additive in the plastic into the liquid medicine or deterioration of the plastic injection device by the liquid medicine. Therefore, it is necessary to pay special attention to the selection of plastic materials for use in an injection device. Furthermore, unlike an injection device made of glass, the water vapor blocking property of an injection device made of plastics is not sufficient and moisture may evaporate, causing a change in the concentration of a liquid medicine.

[0003] Moreover, in a conventional injection device, the plunger rod is equipped with a gasket for a liquid medicine to flow in and out of the syringe. When the sliding resistance between the outer surface of the gasket and the inner surface of the syringe is high, the operation to allow the liquid medicine to flow into or out of the syringe will become difficult. In order to overcome this difficulty, the outer surface of the gasket has been treated with silicone. However, the silicone treatment may result in seepage of the insoluble microparticles of silicone into the liquid medicine.

[0004]

Problems to be Solved by the Invention The present invention was developed in order to eliminate the drawbacks of the conventional plastic injection device mentioned above. Namely, our invention pertains to a plastic injection device with excellent water vapor blocking property with which the

liquid medicine contained in the syringe part of the injection device will not cause seepage of the eluate from the plastics. In addition, the present invention can provide a plastic injection device with low sliding resistance without silicone treatment of the inner surface of the syringe.

[0005] Namely, the present invention pertains to a plastic injection device with its syringe made of a random copolymer of ethylene and a tetracyclo[4.4.0.$1^{2.5}$.$1^{7.10}$-3-dodecene derivative (to be called "TCD" below) (to be called "PETD" below).

[0006] Furthermore, the present invention pertains to the aforementioned plastic injection device, in which the inner surface of the syringe is made of a roughened surface.

[0007] Moreover, the present invention pertains to the aforementioned plastic injection device, in which the gasket is made of polyethylene.

[0008] In addition, the present invention pertains to the aforementioned plastic injection device, in which the outer surface of the gasket is made of a roughened surface.

[0009]

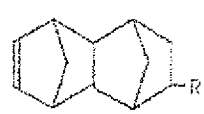
<u>Functions</u> Because the plastic injection device of the present invention is made of PETD with excellent water vapor blocking property, chemical reagent resistance, transparency and size stability, it will not cause seepage of the eluate from plastics into the liquid medicine observed in the conventional injection device made of polypropylene. Moreover, the inner surface of the syringe of the plastic injection device of the present invention is made of a roughened surface to minimize the mutual contact area. Therefore, the flow of the liquid medicine into or out of the syringe can be achieved with low sliding resistance.

[0010]

<u>Actual Examples</u> The PETD used as the plastics of the plastic injection device of the present invention is a random copolymer of ethylene and TCD. TCD is a compound with the chemical structure given below.

[0011]

<u>Chemical Formula 1</u>



[0012] In this formula, R denotes a hydrogen atom or a C_nH_{2n+1} group (n = 1-18).

[0013] The TCD includes, for example, tetracyclo[4.4.0.$1^{2.5}$.$1^{7.10}$-3-dodecene, 8-methyl tetracyclo[4.4.0.$1^{2.5}$.$1^{7.10}$-3-dodecene, 8-ethyl tetracyclo[4.4.0.$1^{2.5}$.$1^{7.10}$-3-dodecene, 8-propyl tetracyclo[4.4.0.$1^{2.5}$.$1^{7.10}$-3-dodecene, 8-butyl tetracyclo[4.4.0.$1^{2.5}$.$1^{7.10}$-3-dodecene, 8-isobutyl tetracyclo[4.4.0.$1^{2.5}$.$1^{7.10}$-3-dodecene, 8-hexyl tetracyclo[4.4.0.$1^{2.5}$.$1^{7.10}$-3-dodecene, 8-stearyl tetracyclo[4.4.0.$1^{2.5}$.$1^{7.10}$-3-dodecene, etc.

[0014] The PETD contains 40-90 mol.% or preferably 50-85 mol.% of the repeating unit derived from ethylene and 10-60 mol.% or preferably 15-50 mol.% of the repeating unit derived from TCD. PETD can be synthesized by polymerizing ethylene and TCD in a hydrocarbon solvent in the presence of a hydrocarbon-soluble vanadium compound and a halogen-containing organic aluminum compound under the conditions described in Unexamined Patent Publication No. Sho 60-[1985]-168,708. The thermal deformation temperature of PETD is in the range of 70-135°C and its transparency is excellent with the haze value in the range of 1-4%. Moreover, the moisture permeability coefficient of PETD is 0.09 g.mm/m^2.24 hr. (measured at 40°C, RH 90%) and its oxygen permeation rate and carbon dioxide permeation rate are 25 cc.mm/m^2.24 hr.atmospheric pressure and 60 cc.mm/m^2.24 hr.atmospheric pressure, respectively. Namely, its permeation rates are 3-5 times smaller than those of polypropylene used in the conventional plastic injection device and it can prevent deterioration of the liquid medicine stored in the syringe for a long time. Such elastic materials as silicone rubber, polyurethane rubber, Clayton rubber, etc., may be added to PETD for improving the impact strength or a lubricating agent may be added for providing a lubricating property.

[0015] It is desirable that the inner surface of the PETD syringe of the present invention is a roughened surface. The roughness of the roughened surface should be greater than 0.1 μm or preferably in the range of 0.3-10 μm or more preferably 0.5-5 μm. When the roughness of the roughened surface is less than 0.1 μm, the syringe inner surface would approach a mirror surface and the area of mutual contact would increase, giving an increasing tendency of the coefficient of friction. As for the shape of the roughened surface, if the front ends are of an acute angle, they would engage with each other, increasing the coefficient of friction. Therefore, it is desirable that front ends are of an obtuse angle so that they can make contact with each other for a sliding motion. The syringe can be formed by extrusion molding or injection molding from a nozzle with roughened inner surface or can be formed by the sandpaper treatment or blast treatment of the mirror-surfaced inner surface of the syringe for roughening of the inner surface.

[0016] Moreover, it is desirable that the outer surface of the gasket sliding on the syringe inner surface is also a roughened surface.

[0017] It is desirable that the gasket is made of such synthetic rubbers as polybutadiene rubber, polyisoprene rubber, etc., elastomers with a hardness greater than that of such soft rubbers as natural rubbers, or thermoplastic resins. It is especially desirable to use such polyethylenes as high density polyethylene, ultrahigh-molecular-weight polyethylene, etc. It is more desirable to use materials with small compression deformation for the gasket used in the PETD syringe of the injection device of the present invention than to use rubbers that may be deformed by compression. The average roughness of the roughened surface should be greater than 0.1 μm or preferably in the range of 0.5-10 μm. When the average roughness of the roughened surface is less than 0.1 μm, the syringe inner surface would approach a mirror surface and the area of mutual contact would increase, giving an increasing tendency of the coefficient of friction.

[0018]

Actual Example 1 Ethylene/tetracyclo[4.4.0.1$^{2.5}$.1$^{7.10}$-3-dodecene copolymer (Apel 6509, a product of Mitsui Petroleum Chemical Co.) was subjected to injection molding to obtain a 10 cc syringe. The syringe inner surface was roughened by sandpaper treatment. The average roughness of the roughened surface was 0.92 μm. Separately, a gasket made of polyethylene with an average molecular weight of 4.5 million (Highzex • Million 340M manufactured by Mitsui Petroleum Chemical Co.) was installed on the front end of a plunger rod made of polypropylene. The outer

surface of the gasket was roughened by the sandpaper treatment. The average roughness of the roughened surface was 0.88 μm. The initial value observed when the plunger equipped with the gasket was inserted into the syringe and the sliding value observed when the plunger was slid in the syringe at a speed of 20 mm/sec were determined. The results are shown in Table 1.

[0019]

Actual Example 2 The initial value observed when the plunger equipped with pretreated gasket without the surface roughening treatment was inserted into the pretreated syringe without surface roughening treatment obtained in Actual Example 1 and the sliding value observed when the plunger was slid in the syringe at a speed of 20 mm/sec. are shown in Table 1.

[0020]

Table 1

		Actual Example 1	Actual Example 2
Sliding resistance, g	Initial value	154	161
	Sliding value	63	71

[0021] It can be seen from Table 1 that the coefficients of friction and the initial value and the sliding value observed with the injection device with surface roughened syringe inner surface and gasket outer surface in Actual Example 1 are smaller than those of the injection device with mirror surfaced syringe inner surface and gasket outer surface in Actual Example 2.

[0022]

Actual Example 3 The PETD used in the syringe of Actual Example 1 was made into a sheet and was subjected to the eluate test according to the Japan Pharmacopoeia "Liquid transporting plastic container test method". The test results are shown in Table 2.

[0023]

Comparison Example 1 Polypropylene (Polypropylene J700N manufactured by Mitsui Petroleum Chemical Co.) was used to form the syringe used in Actual Example 1. This polypropylene was also made into a sheet and was subjected to the eluate test according to the Japan Pharmacopoeia "Liquid transporting plastic container test method". The test results are shown in Table 2.

[0024]

Table 2

		Actual Example 3	Comparison Ex. 1
pH	Test liquid	5.70	5.71
	Blank test liquid	5.85	5.76
	Difference	-0.15	-0.05
Phosphate (comparison liquid PO_4^-) (μg/m*L*)		Inside the limit	Outside the limit
Potassium permanganate reducing substances	Amount of $Na_2S_2O_3$ consumption (test) (g)	19.85	18.60
	Amount of $Na_2S_2O_3$ consumption (blank) (g)	20.00	19.80
	Difference	0.15	1.20
Evaporation residue	Crucible weight (after evaporation to dryness) (g)	19.0220	20.8444
	Crucible weight (before evaporation to dryness) (g)	19.0220	20.8444
	Difference	0.0	0.0
Ultraviolet absorption spectra	241 nm - 350 nm	0.007/241 nm	0.069/257 nm
	220 nm - 240 nm	0.013/220 nm	0.276/220 nm

[0025] It can be seen from Table 2 that the sheet 3 made of PETD used in the syringe of the present invention in Actual Example 3 met all the required items of the eluate test of the Japan Pharmacopoeia "Liquid transporting plastic container test method," but the sheet made of polypropylene used in the syringe in Comparison Example 1 exceeded the threshold values of the test items regarding the ultraviolet absorption spectra, potassium permanganate reducing substance and phosphate.

[0026]

Effects of the Invention The present invention pertains to a plastic injection device with excellent water vapor blocking property, chemical reagent resistance, transparency and size stability. It shows no seepage of the eluate from plastics into a liquid medicine. Furthermore, the inner surface of the syringe and the outer surface of the gasket of the plastic injection device of the present invention are made of a roughened surface and thus this plastic injection device is capable of performing the operation for allowing a liquid medicine to flow into or out of the syringe with low sliding resistance without coating the gasket with a silicone liquid.